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L1: Entry 3 of 8 File: USPT May 29, 2001

DOCUMENT-IDENTIFIER: US 6239133 B1
TITLE: Imidazoquinoxaline protein tyrosine kinase inhibitors

BSPR:
Exemplary such other therapeutic agents include the following: cyclosporins (e.g., cyclosporin A), CTLA4-Ig, antibodies such as anti-ICAM-3, anti-IL-2 receptor (Anti-Tac), anti-CD45RB, anti-CD2, anti-CD3 (OKT-3), anti-CD4, anti-CD80, anti-CD86, monoclonal antibody OKT3, agents blocking the interaction between CD40 and gp39, such as antibodies specific for CD40 and/or gp39 (i.e., CD154), fusion proteins constructed from CD40 and gp39 (CD40Ig and CD8gp39), inhibitors, such as nuclear translocation inhibitors, of NF-kappa B function, such as deoxyspergualin (DSG), non-steroidal antiinflammatory drugs (NSAIDs) such as ibuprofen, steroids such as prednisone or dexamethasone, gold compounds, antiproliferative agents such as methotrexate, FK506 (tacrolimus, Prograf), mycophenolate mofetil, cytotoxic drugs such as azathiprine and cyclophosphamide, TNF-.alpha. inhibitors such as tenidap, anti-TNF antibodies or soluble TNF receptor, and rapamycin (sirolimus or Rapamune) or derivatives thereof, and the PTK inhibitors disclosed in the following U.S. Patent Applications, incorporated herein by reference in their entirety: Ser. No. 60/069,159, filed Dec. 9, 1997 Ser. No. 09/097,338, filed concurrently herewith by Joel C. Barrish et al., "Imidazoquinoxaline Protein Tyrosine Kinase Inhibitors" Ser. No. 60/065,042, filed Nov. 10, 1997, and Ser. No. 60/076,789, filed Mar. 4, 1998. See the following documents and references cited therein: Hollenbaugh, D., Douthwright, J., McDonald, V., and Aruffo, A., "Cleavable CD40Ig fusion proteins and the binding to sgp39", J. Immunol. Methods (Netherlands), 188(1), p. 1-7 (Dec. 15, 1995); Hollenbaugh, D., Grosmaire, L. S., Kullas, C. D., Chalupny, N. J., Braesch-Andersen, S., Noelle, R. J., Stamenkovic, I., Ledbetter, J. A., and Aruffo, A., "The human T cell antigen gp39, a member of the TNF gene family, is a ligand for the CD40 receptor: expression of a soluble form of gp39 with B cell co-stimulatory activity", EMBO J (England), 11(12), p 4313-4321 (December 1992); and Moreland, L. W. et al., "Treatment of rheumatoid arthritis with a recombinant human tumor necrosis factor receptor (p75)-Fc fusion protein, New England J. of Medicine, 337(3), p. 141-147 (1997).

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L1: Entry 6 of 8 File: USPT Nov 23, 1999

DOCUMENT-IDENTIFIER: US 5990109 A
TITLE: Heterocyclo-substituted imidazopyrazine protein tyrosine kinase inhibitors

BSPR:
Exemplary such other therapeutic agents include the following: cyclosporins (e.g., cyclosporin A), CTLA4-Ig, antibodies such as anti-ICAM-3, anti-IL-2 receptor (Anti-Tac), anti-CD45RB, anti-CD2, anti-CD3 (OKT-3), anti-CD4, anti-CD80, anti-CD86, monoclonal antibody OKT3, agents blocking the interaction between CD40 and gp39, such as antibodies specific for CF40 and/or gp39 (i.e., CD154), fusion proteins constructed from CD40 and gp39 (CD40Ig and CD8gp39), inhibitors, such as nuclear translocation inhibitors, of NF-kappa B function, such as deoxyspergualin (DSG), non-steroidal antiinflammatory drugs (NSAIDs) such as ibuprofen, steroids such as prednisone or dexamethasone, gold compounds, antiproliferative agents such as methotrexate, FK506 (tacrolimus, Prograf), mycophenolate mofetil, cytotoxic drugs such as azathiprine and cyclophosphamide, TNF-.alpha. inhibitors such as tenidap, anti-TNF antibodies or soluble TNF receptor, rapamycin (sirolimus or Rapamune), leflunimide (Arava), and cyclooxygenase-2 (COX-2) inhibitors such as celecoxib (Celebrex) and rofecoxib (Vioxx), or derivatives thereof, and the PTK inhibitors disclosed in the following U.S. patent applications, incorporated herein by reference in their entirety: Ser. No. 60/069,159, filed Dec. 9, 1997 (Attorney Docket No. QA202a*), Ser. No. 60/097,338, filed Jun. 15, 1998 (Attorney Docket No. QA202b), Ser. No. 60/056,797, filed Aug. 25, 1997 (Attorney Docket No. QA205*), Ser. No. 09/094,797, filed Jun. 15, 1998 (Attorney Docket No. QA205a), Ser. No. 60/065,042, filed Nov. 10, 1997 (Attorney Docket No. QA207*), and Ser. No. 09/173,413, filed Oct. 15, 1998, (Attorney Docket No. QA207a). See the following documents Ser. No. 60/056,770, filed Aug. 25, 1999 (Attorney Docket No. QA202*), and references cited therein: Hollenbaugh, D., Douthwright, J., McDonald, V., and Aruffo, A., "Cleavable CD40Ig fusion proteins and the binding to sgp39", J. Immunol. Methods (Netherlands), 188(1), p. 1-7 (Dec. 15, 1995); Hollenbaugh, D., Grosmaire, L. S., Kullas, C. D., Chalupny, N. J., Braesch-Andersen, S., Noelle, R. J., Stamenkovic, I., Ledbetter, J. A., and Aruffo, A., "The human T cell antigen gp39, a member of the TNF gene family, is a ligand for the CD40 receptor: expression of a soluble form of gp39 with B cell co-stimulatory activity", EMBO J (England), 11(12), p 4313-4321 (December 1992); and Moreland, L. W. et al., "Treatment of rheumatoid arthritis with a recombinant human tumor necrosis factor receptor (P75)-Fc fusion protein, New England J. of Medicine, 337(3), p. 141-147(1997).

CLPR:
38. The method of claim 27, wherein said compound of the formula I or salt thereof is administered with one or more of: another PTK inhibitor; cyclosporin A; CTLA4-Ig; antibodies selected from anti-ICAM-3, anti-IL-2 receptor (Anti-Tac), anti-CD45RB, anti-CD2, anti-CD3 (OKT-3), anti-CD4, anti-CD80, anti-CD86, and monoclonal antibody OKT3; agents blocking the interaction between CD40 and gp39; fusion proteins constructed from DC40 and gp39; inhibitors of NF-kappa B function; non-steroidal antiinflammatory drugs (NSAIDs); steroids; gold compounds; antiproliferative agents; FK506 (tacrolimus, Prograf); mycophenolate mofetil; cytotoxic drugs; TNF-.alpha. inhibitors; anti-TNF antibodies or soluble TNF receptor; rapamycin (sirolimus or Rapamune); leflunimide (Arava); and cyclooxygenase-2 inhibitors; or derivatives thereof.

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L1: Entry 7 of 8 File: USPT Oct 5, 1999

DOCUMENT-IDENTIFIER: US 5962415 A
TITLE: Compositions comprising a peptide inhibitor of nuclear protein translocation and an immunosuppressant and methods of use thereof

BSPR:
Many immunosuppressants are known in the art to be useful in treating autoimmune disease and in preventing transplant rejection. Examples of known immunosuppressants useful in compositions of the present invention are cyclosporin A, mycophenolate mofetil, rapamycin, FK506, and steroids. Compositions of the present invention comprising at least one peptide inhibitor of nuclear translocation of a protein also comprise at least one immunosuppressant. Together, the peptide inhibitor and immunosuppressant work synergistically to provide better immune suppression than either treatment alone.

DEPR:
The term "immunosuppressant" is used to refer to any compound that is known or found to suppress or prevent an undesired immune response, e.g., prevent the immune system's rejection of a transplanted organ. Examples of "immunosuppressants" include, but are not limited to, cyclosporin A, mycophenolate mofetil, rapamycin, FK506, steroids, and any other known immunosuppressant compound. One or more immunosuppressants may be used in a composition of the present invention.

DEPR:
Since the nuclear translocation of certain cellular peptides is required for the host organism to mount an immune response, the polypeptide inhibitors in combination with other immunosuppressants are useful as immunosuppression compositions. Immune responses are typically manifested by the expression of antibodies, the production of a number of cytokines, and/or the expression of cell surface receptors. Thus, inhibition of immune responses by the compositions of the present invention can take the form of: inhibition of antibody production, including the production of antibody component peptides such as a .kappa. light chain polypeptide; inhibition of cytokine production, including such cytokines as interleukin-1, interleukin-2, interleukin-4, interleukin-6, interleukin-10, tumor necrosis factor, or granulocyte-macrophage colony-stimulating factor; and/or the inhibition of the expression of cell-surface receptors such as an interleukin-2 receptor, gp39, CD40, CD45, CD80, CD86, ICAM, ELAM, major histocompatibility complex ("MHC") class II, or VCAM. Clark et al. (1994) Nature 367:425.

DEPR:
In addition to one or more inhibitory polypeptides, the compositions of the present invention also comprise one or more immunosuppressants. Any known immunosuppressant, for example but not limited to, steroids, mycophenolate mofetil (See, Barry et al. (1996) Drugs 51(2):278-298), rapamycin, FK506, and/or cyclosporin may be used. Preferably, compositions of the present invention comprise cyclosporin alone or in combination with another inmmunosuppressant.

CLPR:
12. The composition of claim 1, wherein said at least one immunosuppressant is selected from the group consisting of cyclosporin, mycophenolate mofetil, steroids, rapamycin, and FK506.

CLPR:
14. The composition of claim 11, wherein said at least one immunosuppressant is selected from the group consisting of cyclosporin, mycophenolate mofetil, steroids, rapamycin and FK506.

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Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences

Search Results -

Term	Documents
CD40L.DWPI,EPAB,JPAB,PGPB.	52
CD40LS	0
CD40.DWPI,EPAB,JPAB,PGPB.	213
CD40S	0
LIGAND.DWPI,EPAB,JPAB,PGPB.	22809
LIGANDS.DWPI,EPAB,JPAB,PGPB.	10407
GP39.DWPI,EPAB,JPAB,PGPB.	38
GP39S	0
5C8.DWPI,EPAB,JPAB,PGPB.	9
5C8S	0
((CD40L OR CD40 ADJ LIGAND OR GP39 OR 5C8) SAME (ANTIBOD$) AND (CYCLOSPORIN$ OR CICLOSPORIN)).PGPB,JPAB,EPAB,DWPI.	5

There are more results than shown above. Click here to view the entire set.

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Refine Search: (cd40L or cd40 adj ligand or gp39 or 5c8) same (antibod$) and (cyclosporin$ or ciclosporin) Clear

Search History

Today's Date: 9/30/2001

DB Name	Query	Hit Count	Set Name
PGPB,JPAB,EPAB,DWPI	(cd40L or cd40 adj ligand or gp39 or 5c8) same (antibod$) and (cyclosporin$ or ciclosporin)	5	L4
PGPB,JPAB,EPAB,DWPI	(cd40L or cd40 adj ligand or gp39 or 5c8) same (antibod$) and rapamycin	2	L3
USPT,PGPB	(cd40L or cd40 adj ligand or gp39 or 5c8) same (antibod$) and immunosuppressive$ same (combination or combined or together)	25	L2
USPT,PGPB	(cd40L or cd40 adj ligand or gp39 or 5c8) same (antibod$) and rapamycin	8	L1

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Main Menu | Search Form | Posting Counts | Show S Numbers | Edit S Numbers | Preferences

Search Results -

Term	Documents
RAPAMYCIN.DWPI,EPAB,JPAB,PGPB.	548
RAPAMYCINS.DWPI,EPAB,JPAB,PGPB.	16
(5 AND RAPAMYCIN).PGPB,JPAB,EPAB,DWPI.	0

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Refine Search: `15 and rapamycin` Clear

Search History

Today's Date: 9/30/2001

DB Name	Query	Hit Count	Set Name
PGPB,JPAB,EPAB,DWPI	15 and rapamycin	0	L6
PGPB,JPAB,EPAB,DWPI	strom-terry$	25	L5
PGPB,JPAB,EPAB,DWPI	(cd40L or cd40 adj ligand or gp39 or 5c8) same (antibod$) and (cyclosporin$ or ciclosporin)	5	L4
PGPB,JPAB,EPAB,DWPI	(cd40L or cd40 adj ligand or gp39 or 5c8) same (antibod$) and rapamycin	2	L3
USPT,PGPB	(cd40L or cd40 adj ligand or gp39 or 5c8) same (antibod$) and immunosuppressive$ same (combination or combined or together)	25	L2
USPT,PGPB	(cd40L or cd40 adj ligand or gp39 or 5c8) same (antibod$) and rapamycin	8	L1

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NFkaapaB
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             514  GP39
            3245  CD40L
           12710  CD40
          290070  LIGAND
            5564  CD40(W)LIGAND
              91  5C8
            1100  CD154
            1646  ANTIBOD?(20N)((((GP39 OR CD40L) OR CD40(W)LIGAND) OR 5C8)
                  OR CD154)
               1  NFKAAPAB
      S8       0  (ANTIBOD?)(20N)(GP39 OR CD40L OR CD40(W)LIGAND OR 5C8 OR
                  CD154) AND NFKAAPAB
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NFkappaB
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             514  GP39
            3245  CD40L
           12710  CD40
          290070  LIGAND
            5564  CD40(W)LIGAND
              91  5C8
            1100  CD154
            1646  ANTIBOD?(20N)((((GP39 OR CD40L) OR CD40(W)LIGAND) OR 5C8)
                  OR CD154)
            5332  NFKAPPAB
      S9       8  (ANTIBOD?)(20N)(GP39 OR CD40L OR CD40(W)LIGAND OR 5C8 OR
                  CD154) AND NFKAPPAB
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...completed examining records
     S10       4  RD S9 (unique items)
? t s10/7/all

 10/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

13202980   BIOSIS NO.: 200100410129
Pathways for self-tolerance and the treatment of autoimmune diseases.
AUTHOR: Goodnow Christopher C(a)
AUTHOR ADDRESS: (a)Australian Cancer Research Foundation, Genetics
  Laboratory, Medical Genome Centre, John Curtin School of Medical
  Research, Australian National University, Canberra, 2601:
  chris.goodnow@anu.edu.au**Australia
JOURNAL: Lancet (North American Edition)  357 (9274):p2115-2121 30 June,
2001
MEDIUM: print
ISSN: 0099-5355
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Antigen delivers both immunogenic and tolerogenic signals to
  lymphocytes. The outcome of antigen exposure represents a complex
  integration of the timing of antigen binding with signals from many other
  immunogenic and tolerogenic costimulatory pathways. A road map of these
  signalling pathways is only beginning to be charted, revealing the
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mechanism of action and limitations of current immunotherapeutic agents and the points of attack for new agents. Ciclosporin and tacrolimus interfere with tolerogenic signals from antigen in addition to blocking immunogenic signals, thus preventing active establishment of tolerance. Corticosteroids inhibit a key immunogenic pathway, **NFkappaB**, and more specific inhibitors of this pathway may allow tolerance to be actively established while immune responses are blocked. New experimental therapies aim to mimic tolerogenic antigen signals by chronically stimulating antigen receptors with antigen or **antibodies** to the receptor, or aim to block costimulatory pathways involving **CD40 ligand**, B7, or interleukin 2. Obtaining the desired response with these strategies is unpredictable because many of these signals have both tolerogenic and immunogenic roles. The cause of autoimmune diseases has been determined for several rare monogenic disorders, revealing inherited deficiencies in tolerogenic costimulatory pathways such as FAS. Common autoimmune disorders may have a biochemically related pathogenesis.

10/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13105314 BIOSIS NO.: 200100312463
Large B cell lymphoma cells utilize A CD40/CD40L/NF-kappaB signalosome for mediating dysregulated cell proliferation.
AUTHOR: Ford Richard J(a); Tamayo Archito(a); Terry Nicholas H(a); Pham Lan (a)
AUTHOR ADDRESS: (a)University of Texas M. D. Anderson Cancer Center, Houston, TX**USA
JOURNAL: Blood 96 (11 Part 1):p335a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Normal human B lymphocyte proliferation is a tightly-regulated process, requiring interaction of the B cell with antigen, antigen presenting cells (APC), and helper (CD4+) T cells, where the antigen-activated T cell transiently expresses the CD40 Ligand (CD40L, CD154, gp39), that in turn activates the B cell. This co-stimulatory pathway activates B cell growth through CD40, a TNF receptor family member, followed by a concatenate array of other signaling molecules that activate the IkappaB-**NFkappaB** complex, that is processed by the proteasome to release the NF-kappaB transcription factor. Neoplastic B cells require a constant source of proliferative signals. High grade B cell lymphomas, from both biopsy cells and cell lines derived from these specimens, show constitutive expression of nuclear NF-kappaB, with normal, non-mutated expression and function of the distal components of the CD40/NF-kappaB pathway. Neoplastic cells accomplish this by assembling inter-connected scaffold-like signaling platform, involving the CD40 pathway referred to as a Signalosome. This CD40 Signalosome, is created by the ectopic production of CD40L by the lymphoma cell that assembles the CD40 pathway into a sub-membrane localized scaffolding structure involving TRAF2, IKKalpha,beta,gamma,IkappaB-NF-kappaB, and the ubiquitination enzyme, E2. This Signalosome can be visualized within individual lymphoma cells using fluorescent antibody labeling with confocal microscopy, where it appears as a granule-like organelle at the internal surface of the cell membrane. The involvement of these components has been confirmed by co-immunoprecipitation and Western blot analysis. Constitutive expression of NF-kappaB can be down-regulated by treatment of the lymphoma cells with a MAb to **CD40L**, that disassembles the Signalosome, blocks lymphoma cell growth, and induces

cell death. Treatment of lymphoma cells with **antibodies** to the concatenate components of the Signalosome also result in disappearance of this scaffolding structure and the corresponding down-regulation of NF-kappaB and cell proliferation. CD40L is not externally secreted by lymphoma cells, but binds to CD40 internally at the cell surface. These studies demonstrate how neoplastic B cells utilize a mechanism similar to their normal B cell counterparts for growth and viability maintenance. The process is dysregulated through ectopic expression and internal binding of the CD40L protein, that provides a continuous activation of the CD40 Signalosome, to mediate neoplastic B cell growth and survival. The Signalosome may in turn provide an interdiction target for therapeutic intervention in the future.

10/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12651794 BIOSIS NO.: 200000405296
Differential effects of cyclosporine A, methylprednisolone, mycophenolate, and rapamycin on CD154 induction and requirement for **NFkappaB**: Implications for tolerance induction.
AUTHOR: Smiley Stephen T; Csizmadia Vilmos; Gao Wei; Turka Laurence A; Hancock Wayne W(a)
AUTHOR ADDRESS: (a)Millennium Pharmaceuticals, Inc., 75 Sidney Street, Cambridge, MA, 02139**USA
JOURNAL: Transplantation (Baltimore) 70 (3):p415-419 August 15, 2000
MEDIUM: print
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Background: Recent experimental data indicate that the targeting of the costimulatory molecule CD40-ligand (CD154) may well offer an opportunity for tolerance induction in transplant recipients and patients with autoimmune diseases, although the optimal therapeutic strategy for clinical application of **CD154** monoclonal **antibody** (mAb) is unclear. Methods: We undertook vascularized heterotopic cardiac allograft transplantation in completely MHC-mismatched mice, treated recipients with **CD154** mAb plus various immunosuppressive agents, and performed flow cytometric analysis of CD154 expression by T cells activated in vitro in the presence of corresponding immunosuppressive agents. We also tested the extent to which CD154 induction was **NFkappaB**-dependent by using **NFkappaB**/p50-deficient mice as allograft recipients and as source of cells for in vitro studies of CD154 induction, and through use of proteasome inhibitors to block IkappaBalpha degradation and **NFkappaB** activation in wild-type mice. Results: Concomitant use of cyclosporin A or methylprednisolone, but not rapamycin or mycophenolate, inhibited CD154 mAb-induced allograft survival. The differential effects of these agents on CD154 mAb-induced tolerance correlated with their capacity to inhibit activation-induced CD154 expression on CD4+ T cells. Full expression of CD154 expression was found to require NF-kappaB activation, and CD154 mAb was ineffective in NF-kappaB/p50 deficient allograft recipients or control mice in which NF-kappaB activation was blocked by proteasome inhibition. Conclusions: Strategies to use CD154 mAb clinically must take into account the effects of immunosuppressive agents on CD154 induction, which seems to be at least partially NF-kappaB dependent. Our data suggest that ligation of surface-expressed CD154 provides an important signal that modulates T cell activation and thereby contributes to the effects of CD154 mAb, in addition to previously recognized actions involving blockade of CD40/CD154-dependent cell activation and activation-induced cell death.

10/7/4 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

122237203 CA: 122(19)237203u JOURNAL
Agonistic and antagonistic properties of CD40 mAb G28-5 are dependent on binding valency
AUTHOR(S): Ledbetter, Jeffrey A.; Grosmaire, Laura S.; Hollenbaugh, Diane ; Aruffo, Alejandro; Nadler, Steven G.
LOCATION: Pharmaceutical Research Institute, Bristol-Myers Squibb, Seattle, WA, USA
JOURNAL: Circ. Shock DATE: 1994 VOLUME: 44 NUMBER: 2 PAGES: 67-72
CODEN: CRSHAG ISSN: 0092-6213 LANGUAGE: English
SECTION:
CA215002 Immunochemistry
IDENTIFIERS: CD40 antibody NFkappaB gp39 signal transduction
DESCRIPTORS:
Antigens,CD40... Cell proliferation... Glycoproteins,specific or class, gp39... Immunoglobulins,G1, monoclonal... Lymphocyte,B-cell... Ribonucleic acid formation factors,NF-.kappa.B (nuclear factor .kappa.B)... Signal transduction,biological...
agonistic and antagonistic properties of CD40 monoclonal antibody in relation to gp39 binding and NF-.kappa.B activation
Receptors...
for CD40; agonistic and antagonistic properties of CD40 monoclonal antibody in relation to gp39 binding and NF-.kappa.B activation
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  File 155:MEDLINE(R)  1966-2001/Oct W3
  File 399:CA SEARCH(R)  1967-2001/UD=13514
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*File 399: Use is subject to the terms of your user/customer agreement.
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E7       18  AU=STROM TIM M
E8       30  AU=STROM TM
E9        1  AU=STROM TORBJORN
E10       1  AU=STROM U
E11      18  AU=STROM V
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 3/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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13123514   BIOSIS NO.: 200100330663
Adjunctive rapamycin and CsA treatment inhibits monocyte/macrophage
  associated cytokines/chemokines in sensitized cardiac graft recipients.
AUTHOR: Wasowska Barbara A(a); Zheng X X; Strom Terry B;
  Kupiec-Weglinski Jerzy W
AUTHOR ADDRESS: (a)Department of Pathology, The Johns Hopkins School of
  Medicine, 720 Rutland Avenue, Ross No. 664H, Baltimore, MD, 21205**USA
JOURNAL: Transplantation (Baltimore)  71 (8):p1179-1183 April 27, 2001
MEDIUM: print
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English


 3/3/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

12751129   BIOSIS NO.: 200000504752
Rapamycin induces transforming growth factor-beta production by
  lymphocytes.
AUTHOR: Dodge Ingrid L; Demirci Gulcin; Strom Terry B; Li Xian Chang
  (a
AUTHOR ADDRESS: (a)Department of Medicine, Division of Immunology, Beth
  Israel Deaconess Medical Center, Boston, MA, 02215**USA
JOURNAL: Transplantation (Baltimore)  70 (7):p1104-1106 October 15, 2000
MEDIUM: print
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English


 3/3/3     (Item 3 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

12280260   BIOSIS NO.: 200000033762
Requirement for T-cell apoptosis in the induction of peripheral
  transplantation tolerance.
AUTHOR: Wells Andrew D; Li Xian Chang; Li Yongsheng; Walsh Matthew C; Zheng
```

Xin Xiao; Wu Zihao; Nunez Gabriel; Tang Aimin; Sayegh Mohamed; Hancock Wayne W; **Strom Terry B**; Turka Laurence A(a
AUTHOR ADDRESS: (a)Department of Medicine, University of Pennsylvania, Philadelphia, PA, 19104**USA
JOURNAL: Nature Medicine 5 (11):p1303-1307 Nov., 1999
ISSN: 1078-8956
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

3/3/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12280259 BIOSIS NO.: 200000033761
Blocking both signal 1 and signal 2 of T-cell activation prevents apoptosis of alloreactive T cells and induction of peripheral allograft tolerance.
AUTHOR: Li Yongsheng; Li Xian Chang; Zheng Xin Xiao; Wells Andrew D; Turka Laurence A; **Strom Terry B**(a
AUTHOR ADDRESS: (a)Department of Medicine, Harvard Medical School, Division of Immunology, Beth Israel Deaconess Medical Center, Boston, MA, 02215** USA
JOURNAL: Nature Medicine 5 (11):p1298-1302 Nov., 1999
ISSN: 1078-8956
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

3/3/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11797525 BIOSIS NO.: 199900043634
Combined costimulation blockade plus **rapamycin** but not cyclosporine produces permanent engraftment.
AUTHOR: Li Yongsheng; Zheng Xin Xiao; Li Xian Chang; Zand Martin S; **Strom Terry B**(a
AUTHOR ADDRESS: (a)Div. Immunol., Beth Israel Deaconess Med. Center, P.O. Box 15707, Boston, MA 02215**USA
JOURNAL: Transplantation (Baltimore) 66 (10):p1387-1388 Nov. 27, 1998
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11773118 BIOSIS NO.: 199900019227
Rapamycin but not cyclosporine preserves the beneficial effects of costimulation blockade.
AUTHOR: Li Yongsheng; Zheng Xin Xiao; Li Xan Chang; Zand Martin S; **Strom Terry B**
AUTHOR ADDRESS: Harv. Med. Sch., Beth Isr. Deaconess Med. Cent., Boston, MA**USA
JOURNAL: Journal of the American Society of Nephrology 9 (PROGRAM AND ABSTR. ISSUE):p654A Sept., 1998
CONFERENCE/MEETING: 31st Annual Meeting of the American Society of Nephrology Philadelphia, Pennsylvania, USA October 25-28, 1998
SPONSOR: American Society of Nephrology

ISSN: 1046-6673
RECORD TYPE: Citation
LANGUAGE: English

3/3/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11169858 BIOSIS NO.: 199799791003
Immunoregulatory drugs: Mechanistic basis for use in organ transplantation.
AUTHOR: Suthanthiran Manikkam(a); **Strom Terry B**
AUTHOR ADDRESS: (a)525 East 68th St., Box 3, New York, NY 10021**USA
JOURNAL: Pediatric Nephrology 11 (5):p651-657 1997
ISSN: 0931-041X
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

3/3/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10178361 BIOSIS NO.: 199698633279
Cytokine and alloantibody networks in long term cardiac allografts in rat recipients treated with **rapamycin**.
AUTHOR: Wasowska Barbara; Wieder Kenneth J; Hancock Wayne W; Zheng Xin Xiao ; Berse Brygida; Binder Jochen; **Strom Terry B**; Kupiec-Weglinski Jerzy W(a
AUTHOR ADDRESS: (a)Surg. Res. Lab., Harvard Med. Sch., 260 Longwood Ave., Boston, MA 02115**USA
JOURNAL: Journal of Immunology 156 (1):p395-404 1996
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09368169 BIOSIS NO.: 199497376539
Quantitative comparison of **rapamycin** and cyclosporine effects on cytokine gene expression studied by reverse transcriptase-competitive polymerase chain reaction.
AUTHOR: Zheng Xin Xiao; **Strom Terry B**; Steele Alan W(a
AUTHOR ADDRESS: (a)Dep. Med., Beth Israel Hosp., 330 Brookline Ave., Boston, MA 02215**USA
JOURNAL: Transplantation (Baltimore) 58 (1):p87-92 1994
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08928024 BIOSIS NO.: 199396079525
Rapamycin treatment depresses intragraft expression of KC/MIP-2, granzyme B, and IFN-gamma in rat recipients of cardiac allografts.
AUTHOR: Wieder Kenneth J; Hancock Wayne W; Schmidbauer Georg; Corpier Cindy L; Wieder Irene; Kobzik Lester; **Strom Terry B**; Kupiec-Weglinski

Jerzy W(a
AUTHOR ADDRESS: (a)Surgical Res. Lab., Harvard Med. Sch., 260 Longwood Ave., Boston, MA 02115**USA
JOURNAL: Journal of Immunology 151 (2):p1158-1166 1993
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

3/3/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08709615 BIOSIS NO.: 199345127690
Quantitative comparison of immunoregulatory effects of **rapamycin** and cyclosporine on cytokine gene transcription.
AUTHOR: Zheng Xin Xiao(a); Steele Alan W; **Strom Terry B**
AUTHOR ADDRESS: (a)Div. Immunol., Beth Israel Hosp., Harvard Med. Sch., Boston, MA**USA
JOURNAL: Journal of the American Society of Nephrology 4 (3):p921 1993
CONFERENCE/MEETING: 26th Annual Meeting of the ASN (American Society of Nephrology) Boston, Massachusetts, USA November 14-17, 1993
ISSN: 1046-6673
RECORD TYPE: Citation
LANGUAGE: English

3/3/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08467229 BIOSIS NO.: 199344017229
Transcription of interleukin-8-like and cytotoxic T-cell-specific serine esterase genes in allograft recipients is prevented by **rapamycin** treatment.
AUTHOR: Schmidbauer Georg(a); Wieder Kenneth J; Corpier Cindy L; Wieder Irene; Sablinski Thomasz; **Strom Terry B**; Kupiec-Weglinski Jerzy W
AUTHOR ADDRESS: (a)Harvard Med. Sch., Div. Clin. Immunol., Beth Isr. Hosp., Boston, Mass.**USA
JOURNAL: Surgical Forum 43 (0):p416-419 1992
CONFERENCE/MEETING: 48th Annual Sessions of the Forum on Fundamental Surgical Problems held at the 78th Clinical Congress of the American College of Surgeons, New Orleans, Louisiana, USA, October 11-16, 1992. SURG FORUM
ISSN: 0071-8041
DOCUMENT TYPE: Article
RECORD TYPE: Citation
LANGUAGE: English
? ds

Set	Items	Description
S1	102	E1-E5
S2	12	S1 AND RAPAMYCIN
S3	12	RD S2 (unique items)

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? s s1 and (gp39 or cd40L or cd40(w)ligand or 5c8 or cd154)
             102  S1
             514  GP39
            3245  CD40L
           12710  CD40
          290070  LIGAND
            5564  CD40(W)LIGAND
              91  5C8
            1100  CD154
      S4       3  S1 AND (GP39 OR CD40L OR CD40(W)LIGAND OR 5C8 OR CD154)
? rd s4
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...completed examining records
S5 3 RD S4 (unique items)
? t s5/3/all

5/3/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12280259 BIOSIS NO.: 200000033761
Blocking both signal 1 and signal 2 of T-cell activation prevents apoptosis of alloreactive T cells and induction of peripheral allograft tolerance.
AUTHOR: Li Yongsheng; Li Xian Chang; Zheng Xin Xiao; Wells Andrew D; Turka Laurence A; **Strom Terry B**(a
AUTHOR ADDRESS: (a)Department of Medicine, Harvard Medical School, Division of Immunology, Beth Israel Deaconess Medical Center, Boston, MA, 02215** USA
JOURNAL: Nature Medicine 5 (11):p1298-1302 Nov., 1999
ISSN: 1078-8956
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

5/3/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11797525 BIOSIS NO.: 199900043634
Combined costimulation blockade plus rapamycin but not cyclosporine produces permanent engraftment.
AUTHOR: Li Yongsheng; Zheng Xin Xiao; Li Xian Chang; Zand Martin S; **Strom Terry B**(a
AUTHOR ADDRESS: (a)Div. Immunol., Beth Israel Deaconess Med. Center, P.O. Box 15707, Boston, MA 02215**USA
JOURNAL: Transplantation (Baltimore) 66 (10):p1387-1388 Nov. 27, 1998
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

5/3/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11773118 BIOSIS NO.: 199900019227
Rapamycin but not cyclosporine preserves the beneficial effects of costimulation blockade.
AUTHOR: Li Yongsheng; Zheng Xin Xiao; Li Xan Chang; Zand Martin S; **Strom Terry B**
AUTHOR ADDRESS: Harv. Med. Sch., Beth Isr. Deaconess Med. Cent., Boston, MA**USA
JOURNAL: Journal of the American Society of Nephrology 9 (PROGRAM AND ABSTR. ISSUE):p654A Sept., 1998
CONFERENCE/MEETING: 31st Annual Meeting of the American Society of Nephrology Philadelphia, Pennsylvania, USA October 25-28, 1998
SPONSOR: American Society of Nephrology
ISSN: 1046-6673
RECORD TYPE: Citation
LANGUAGE: English
? s (antibod?)(20n)(gp39 or cd40L or cd40(w)ligand or 5c8 or cd154) and rapamycin
1647344 ANTIBOD?
514 GP39
3245 CD40L

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          12710  CD40
         290070  LIGAND
           5564  CD40(W)LIGAND
             91  5C8
           1100  CD154
           1646  ANTIBOD?(20N)((((GP39 OR CD40L) OR CD40(W)LIGAND) OR 5C8)
                 OR CD154)
           7847  RAPAMYCIN
      S6      8  (ANTIBOD?)(20N)(GP39 OR CD40L OR CD40(W)LIGAND OR 5C8 OR
                 CD154) AND RAPAMYCIN
? rd s6
...completed examining records
      S7      5  RD S6 (unique items)
? t s7/7/all

 7/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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12651794   BIOSIS NO.: 200000405296
Differential effects of cyclosporine A, methylprednisolone, mycophenolate,
  and rapamycin on CD154 induction and requirement for NFkappaB:
  Implications for tolerance induction.
AUTHOR: Smiley Stephen T; Csizmadia Vilmos; Gao Wei; Turka Laurence A;
  Hancock Wayne W(a)
AUTHOR ADDRESS: (a)Millennium Pharmaceuticals, Inc., 75 Sidney Street,
  Cambridge, MA, 02139**USA
JOURNAL: Transplantation (Baltimore)  70 (3):p415-419 August 15, 2000
MEDIUM: print
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Background: Recent experimental data indicate that the targeting
  of the costimulatory molecule CD40-ligand (CD154) may well offer an
  opportunity for tolerance induction in transplant recipients and patients
  with autoimmune diseases, although the optimal therapeutic strategy for
  clinical application of CD154 monoclonal antibody (mAb) is
  unclear. Methods: We undertook vascularized heterotopic cardiac allograft
  transplantation in completely MHC-mismatched mice, treated recipients
  with CD154 mAb plus various immunosuppressive agents, and performed
  flow cytometric analysis of CD154 expression by T cells activated in
  vitro in the presence of corresponding immunosuppressive agents. We also
  tested the extent to which CD154 induction was NFkappaB-dependent by
  using NFkappaB/p50-deficient mice as allograft recipients and as source
  of cells for in vitro studies of CD154 induction, and through use of
  proteasome inhibitors to block IkappaBalpha degradation and NFkappaB
  activation in wild-type mice. Results: Concomitant use of cyclosporin A
  or methylprednisolone, but not rapamycin or mycophenolate,
  inhibited CD154 mAb-induced allograft survival. The differential effects
  of these agents on CD154 mAb-induced tolerance correlated with their
  capacity to inhibit activation-induced CD154 expression on CD4+ T cells.
  Full expression of CD154 expression was found to require NF-kappaB
  activation, and CD154 mAb was ineffective in NF-kappaB/p50 deficient
  allograft recipients or control mice in which NF-kappaB activation was
  blocked by proteasome inhibition. Conclusions: Strategies to use CD154
  mAb clinically must take into account the effects of immunosuppressive
  agents on CD154 induction, which seems to be at least partially NF-kappaB
  dependent. Our data suggest that ligation of surface-expressed CD154
  provides an important signal that modulates T cell activation and thereby
  contributes to the effects of CD154 mAb, in addition to previously
  recognized actions involving blockade of CD40/CD154-dependent cell
  activation and activation-induced cell death.
```

7/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11773118 BIOSIS NO.: 199900019227
Rapamycin but not cyclosporine preserves the beneficial effects of costimulation blockade.
AUTHOR: Li Yongsheng; Zheng Xin Xiao; Li Xan Chang; Zand Martin S; Strom Terry B
AUTHOR ADDRESS: Harv. Med. Sch., Beth Isr. Deaconess Med. Cent., Boston, MA**USA
JOURNAL: Journal of the American Society of Nephrology 9 (PROGRAM AND ABSTR. ISSUE):p654A Sept., 1998
CONFERENCE/MEETING: 31st Annual Meeting of the American Society of Nephrology Philadelphia, Pennsylvania, USA October 25-28, 1998
SPONSOR: American Society of Nephrology
ISSN: 1046-6673
RECORD TYPE: Citation
LANGUAGE: English

7/7/3 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11022750 EMBASE No: 2000122918
Transplantation
Gonwa T.A.
Dr. T.A. Gonwa, Baylor University Medical Center, 3500 Gaston Ave, Dallas, TX 75246 United States
AUTHOR EMAIL: TGONWA@EARTHLINK.NET
American Journal of Kidney Diseases (AM. J. KIDNEY DIS.) (United States) 2000, 35/4 SUPPL. 1 (S153-S159)
CODEN: AJKDD ISSN: 0272-6386
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 43

The history of solid organ transplantation is traced from its beginnings in the 19th century to the beginning of the 21st century. Surgical techniques, advances in immunology, and a review of major immunosuppressive milestones are reviewed. Over the last 50 years, transplantation has moved from experimental to accepted clinical therapy. The technology of transplantation has been widely disseminated throughout the United States. This paper reviews the major ethical and social problems that still need to be addressed in regards to transplantation. These include organ supply, organ distribution, access to care, funding, and xenotransplantation. (C) 2000 by the National Kidney Foundation, Inc.

7/7/4 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

10512730 EMBASE No: 1999423839
New immunosuppressive agents in renal transplantation
NUOVI AGENTI IMMUNOSOPPRESSORI NEL TRAPIANTO
Ponticelli C.; Montagnino G.
Prof. C. Ponticelli, Divisione di Nefrologia e Dialisi, Ospedale Maggiore IRCCS, Via Commenda 15, 20122 Milano Italy
Giornale Italiano di Nefrologia (G. ITAL. NEFROL.) (Italy) 1999, 16/2 (180-185)
CODEN: GINEE ISSN: 0393-5590
DOCUMENT TYPE: Journal; Article
LANGUAGE: ITALIAN SUMMARY LANGUAGE: ENGLISH; ITALIAN

NUMBER OF REFERENCES: 60

Among the more recent immunosuppressive agents, Sirolimus and monoclonal antibodies directed against the IL-2 receptor are the most promising. Sirolimus inhibits the Ginf 1-S phase of the cell cycle, at a later stage than calcineurin inhibitors, which interfere with the Ginf 0-Ginf 1 phase. Clinical studies have demonstrated the efficacy of Sirolimus in reducing the risk of rejection when combined with CsA and steroids. Sirolimus also proved to be effective as an alternative to CsA. The monoclonal antibodies directed against the IL-2 receptor significantly reduce the risk of acute rejection without side-effects. Other immunosuppressive agents are still being assessed in phase I-H clinical studies. FTY 720 may induce selective apoptosis of lymphocytes reacting against the donor's alloantigens. Antisense oligonucleotides interfere with adhesion molecules, while the monoclonal antibodies CTLA4-Ig and 5C-8 interfere with the co-stimulatory signals between the antigen presenting cell and the lymphocyte. An ever increasing number of new immunosuppressive agents is becoming available. The difficult task of the clinician is to find the right equilibrium in dosing and associating these new drugs in order to maximize the therapeutic effect of immunosuppressive treatment.

7/7/5 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09484851 94298104 PMID: 7517796
Inhibition of human B lymphocyte cell cycle progression and differentiation by **rapamycin**.
Aagaard-Tillery KM; Jelinek DF
Department of Immunology, Mayo Clinic/Foundation, Rochester, Minnesota 55905.
Cellular immunology (UNITED STATES) Jul 1994, 156 (2) p493-507, ISSN 0008-8749 Journal Code: CQ9
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
In this study, we have analyzed the effects of the immunosuppressive agent **rapamycin** on the activation of highly purified normal human B lymphocytes. When the polyclonal activators Staphylococcus aureus (SA) and soluble CD40 ligand (CD40L) were used to stimulate B cells, **rapamycin** inhibited both interleukin 2 (IL2)-dependent and -independent proliferation, as well as IL2-dependent differentiation into antibody-secreting cells. Cell cycle analysis indicated that **rapamycin** inhibited the progression of SA+IL2-stimulated B cells past the mid-G1 phase of the cell cycle. To begin to identify **rapamycin** -sensitive signaling events essential for B cell activation, we examined the effects of **rapamycin** on p34cdc2 and p33cdk2 kinase activities. SA+IL2 stimulation induced the activation of both cyclin-dependent kinases. Of interest, **rapamycin** abrogated the activation of both p34cdc2 and p33cdk2. Our results indicate therefore that **rapamycin** inhibits a number of SA- and CD40L-inducible events that may be necessary for both entry into S phase and for permitting subsequent B cell differentiation. These studies emphasize the utility of this drug as a tool to begin to dissect the activation pathways utilized by human B cells, as well as to provide implications for the therapeutic use of **rapamycin** in vivo.
Record Date Created: 19940811